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=> save all
ENTER NAME OR (END):l09987930/l
L# LIST L1-L23 HAS BEEN SAVED AS 'L09987930/L'

=> d his

     (FILE 'HOME' ENTERED AT 14:00:54 ON 17 SEP 2003)

     FILE 'REGISTRY' ENTERED AT 14:01:02 ON 17 SEP 2003

     FILE 'CAPLUS' ENTERED AT 14:01:09 ON 17 SEP 2003
L1             1 S WO9937305/PN
                 SELECT L1 1 RN

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L2             1 S E1
L3             1 S E2
L4             1 S E3
L5             1 S E4
L6             1 S E5
L7             1 S E6
L8             1 S E7
L9             1 S E8
L10            1 S E9
L11            1 S E10

     FILE 'CAPLUS' ENTERED AT 14:04:11 ON 17 SEP 2003
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                 SELECT L12 1 RN

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L15            1 S E36
L16            1 S E37
L17            1 S E38
L18            1 S E40
L19            1 S E51
L20            1 S E30
L21            1 S E19
L22            1 S E12
L23            1 S E26
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E1           1     106083-71-0/BI
E2           1     124-68-5/BI
E3           1     15481-39-7/BI
E4           1     192374-14-4/BI
E5           1     192374-15-5/BI
E6           1     233600-52-7/BI
E7           1     233600-53-8/BI
E8           1     233600-54-9/BI
E9           1     34841-35-5/BI
E10          1     34911-51-8/BI
E11          2     109889-09-0/BI
E12          2     112727-80-7/BI
E13          2     34911-55-2/BI
E14          2     364-62-5/BI
E15          2     83863-69-8/BI
E16          2     89565-68-4/BI
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E18          2     99614-02-5/BI
E19          1     102141-11-7/BI
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E40	1	357628-62-7/BI
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E42	1	357628-64-9/BI
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E44	1	357637-18-4/BI
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E46	1	386210-40-8/BI
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E48	1	50-67-9/BI
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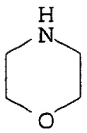
E54	1	87-69-4/BI
E55	1	92264-81-8/BI
E56	1	92264-82-9/BI
E57	1	99102-04-2/BI

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 146420-18-0 REGISTRY
CN **Morpholinol (9CI)** (CA INDEX NAME)
MF C4 H9 N O2
CI IDS
SR CA
LC STN Files: BIOSIS, CA, CAPLUS



D1—OH

2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

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E50             1      51-61-6/BI
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E52             1      80478-43-9/BI
E53             1      82801-49-8/BI
E54             1      87-69-4/BI
E55             1      92264-81-8/BI
E56             1      92264-82-9/BI
E57             1      99102-04-2/BI

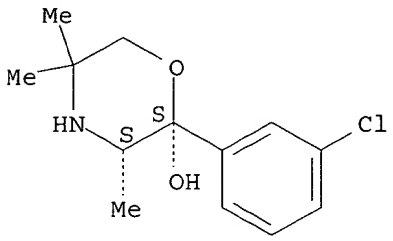

=>
```

L16 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **357399-44-1** REGISTRY
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)-, (2R,3R)-2,3-bis[(4-methylbenzoyl)oxy]butanedioate (1:1) (salt) (9CI)
FS STEREOSEARCH
MF C20 H18 O8 . C13 H18 Cl N O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

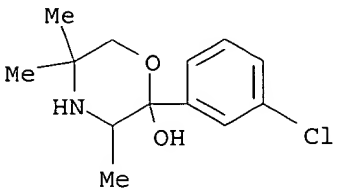
CRN 192374-14-4
CMF C13 H18 Cl N O2

Absolute stereochemistry. Rotation (+).



CM 2

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **357399-43-0** REGISTRY
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Hydroxy-2-(3-chlorophenyl)-3,5,5-trimethylmorpholine
FS 3D CONCORD
MF C13 H18 Cl N O2
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

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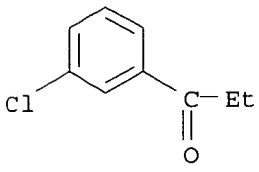
L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **34841-35-5** REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Propiophenone, 3'-chloro- (6CI, 7CI)
OTHER NAMES:
CN 1-(3-Chlorophenyl)-1-propanone
CN 3-Chlorophenyl ethyl ketone
CN m-Chloropropiophenone
FS 3D CONCORD
MF C9 H9 Cl O
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, PROMT, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

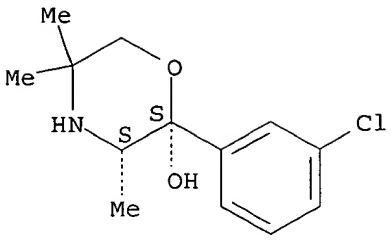
44 REFERENCES IN FILE CA (1937 TO DATE)
44 REFERENCES IN FILE CAPLUS (1937 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s e21
L14 1 106083-71-0/BI

=> d

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **106083-71-0** REGISTRY
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, [S-(R*,R*)]-
OTHER NAMES:
CN BW 306U
FS STEREOSEARCH
MF C13 H18 Cl N O2 . Cl H
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, TOXCENTER, USPAT2, USPATFULL
CRN (192374-14-4)

Absolute stereochemistry. Rotation (+).

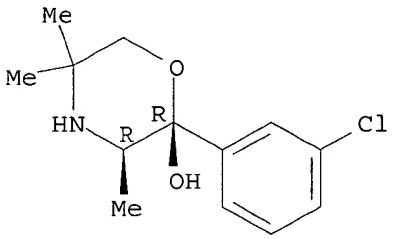


● HCl

9 REFERENCES IN FILE CA (1937 TO DATE)
9 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L23 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **192374-15-5** REGISTRY
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R-cis)-
OTHER NAMES:
CN (-)-(2R,3R)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol
FS STEREOSEARCH
MF C13 H18 Cl N O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1937 TO DATE)
9 REFERENCES IN FILE CAPLUS (1937 TO DATE)

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L25 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:334659 CAPLUS
DN 138:343887
TI Pharmaceutical compositions containing morpholinol deriv.
IN Partridge, John Joseph
PA USA
SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. 6,391,875.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-535
NCL 514238800
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 4, 31
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003083330	A1	20030501	US 2002-150287	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		

AB A compn. contains (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (I) and salts and solvates thereof. A method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, addiction to cocaine or nicotine-contg. (esp. tobacco) products, or addiction to alc. using such a compd. is also disclosed. Results from the tetrabenazine-induced behavioral depression model showed that in vivo at 25 mg/kg (i.p.), I and the racemate, abolished the tetrabenazine-induced behavioral depression. In contrast, the (-) enantiomer of I showed only modest activity.

ST morpholinol pharmaceutical antidepressant alcoholism prepn; chlorophenyltrimethylmorpholinol pharmaceutical alcoholism prepn

IT Absolute configuration
Alcoholism
Antidepressants
Drug delivery systems
(pharmaceutical compns. contg. morpholinol deriv.)

IT Synapse
(synaptosome; pharmaceutical compns. contg. morpholinol deriv.)

IT **233600-52-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

IT **192374-15-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

IT **233600-54-9P** 517866-72-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

IT **106083-71-0P 192374-14-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. contg. morpholinol deriv.)

IT **233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmaceutical compns. contg. morpholinol deriv.)

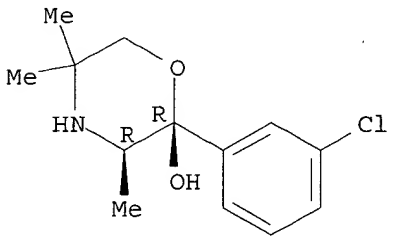
IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(uptake; pharmaceutical compns. contg. morpholinol deriv.)

IT **233600-52-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 233600-52-7 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

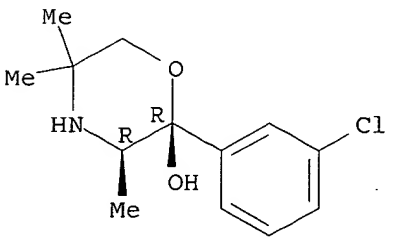


IT **192374-15-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



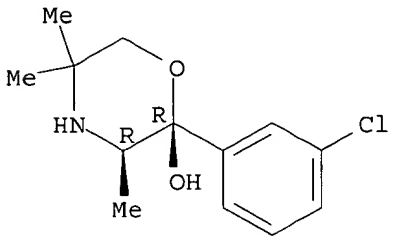
IT **233600-54-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 233600-54-9 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

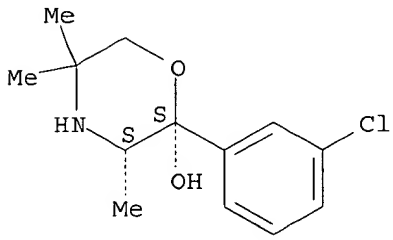
IT **106083-71-0P 192374-14-4P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. contg. morpholinol deriv.)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

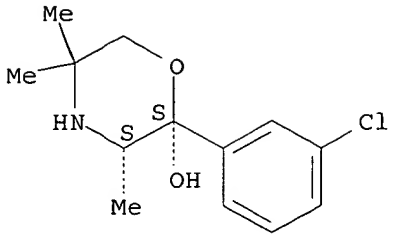


● HCl

RN 192374-14-4 CAPLUS

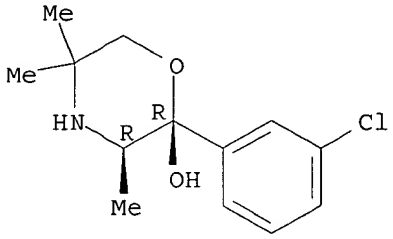
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmaceutical compns. contg. morpholinol deriv.)
RN 233600-53-8 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L25 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:261022 CAPLUS
DN 138:265672
TI Pharmaceutically active morpholinol, preparation, pharmaceutical compositions, and therapeutic use
IN Morgan, Phillip Frederick; Musso, David Lee; Partridge, John Joseph
PA USA
SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. 6,391,875.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-537
NCL 514238800
CC 1-11 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003064988	A1	20030403	US 2002-150339	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		

AB The invention discloses the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and processes for their prepn. and use. Also disclosed is a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, or addiction to cocaine or nicotine-contg. (esp. tobacco) products using the above compd., salts, solvates, or compns. The compd. of the invention (prepn. and resoln. described) is an enantiomer of a bupropion metabolite.

ST bupropion metabolite enantiomer morpholinol deriv prepn pharmaceutical; attention deficit hyperactivity disorder morpholinol deriv; depression obesity migraine pain morpholinol deriv; sexual dysfunction Parkinson disease morpholinol deriv; Alzheimer disease cocaine addiction morpholinol deriv; tobacco nicotine product addiction morpholinol deriv

IT Mental disorder
(bipolar disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Analgesics
Antidepressants
Antimigraine agents
Antiparkinsonian agents
Pain
Parkinson's disease
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Resolution (separation)
(chromatog.; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Mental disorder
(depression; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Sexual behavior
(disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Toxicity
(drug; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Behavior
(locomotor, disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Mental disorder
(major depression; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Headache
(migraine; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Behavior
(motor, disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Nerve, disease
(neuropathy, neuropathic pain; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Drug dependence
(nicotine-contg. product; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Biological transport
(uptake, sexual dysfunction as selective serotonin reuptake inhibitor-class antidepressant side effect; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **233600-52-7P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **192374-15-5P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **192374-14-4P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 31677-93-7, Wellbutrin 34911-55-2, Bupropion
RL: PAC (Pharmacological activity); BIOL (Biological study)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **106083-71-0P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **233600-54-9P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone **233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

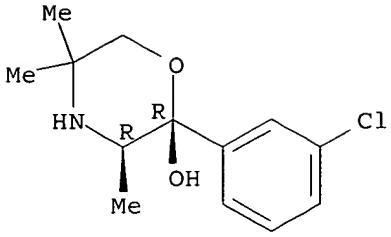
IT 54-11-5, Nicotine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(nicotine-contg. product addiction; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(uptake; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **233600-52-7P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

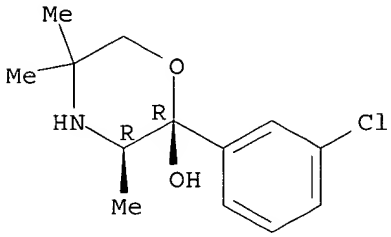
RN 233600-52-7 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



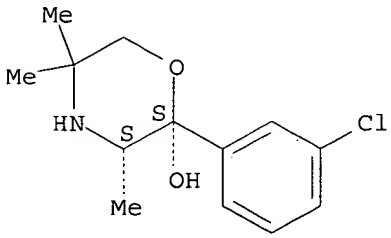
IT **192374-15-5P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)
RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **192374-14-4P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)
RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

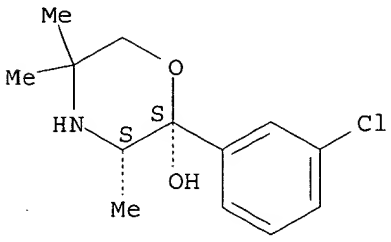
Absolute stereochemistry. Rotation (+).



IT **106083-71-0P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 106083-71-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

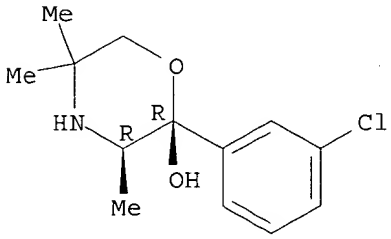
Absolute stereochemistry. Rotation (+).



● HCl

IT **233600-54-9P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)
RN 233600-54-9 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

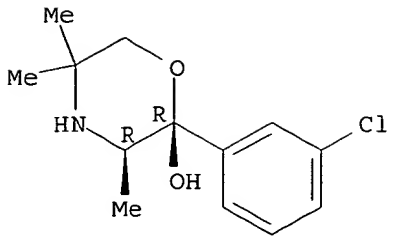
Absolute stereochemistry. Rotation (-).



● HCl

IT **233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)
RN 233600-53-8 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L25 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:173828 CAPLUS
DN 138:218798
TI Polymorphisms in genes associated with norepinephrine function and their use in the design and selection of therapies
IN Dow, David J.; Duncan, Ben; Hughes, Arlene R.; Manasco, Penelope; Pillai, Sreekumar G.; Spaulding, Theodore C.; Spraggs, Colin F.; Stubbins, Michael; Xu, Chun-Fang
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
ICS C07H021-04
CC 13-6 (Mammalian Biochemistry)
Section cross-reference(s): 1, 3
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003018843	A1	20030306	WO 2002-US25060	20020807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003100479	A1	20030529	US 2002-213948	20020807
PRAI US 2001-313918P	P	20010821		
US 2001-337819P	P	20011108		

AB Correlations between the appearance of polymorphisms in various genes and a subject's phenotypic response to treatment with a norepinephrine reuptake inhibitor are described. Methods of screening subjects to aid in the medical treatment of obesity are presented. Polymorphisms are described in genes for monoamine oxidase B, the NET1 norepinephrine transporter, the DAT1 dopamine transporter, the D2 dopamine receptor, the serotonin transporter and the NR1 NMDA receptor. Clin. studies between the effectiveness of the antiobesity agents GW320659 and GW353162 and genotypes at these loci are presented.
ST obesity norepinephrine reuptake polymorphism obesity treatment
IT Dopamine receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(D2, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G155A, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G6435A, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal
Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NET1, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA-binding, NMDAR-1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NR1, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(T342C, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Repetitive DNA
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VNTR (variable-no. tandem-repeat), polymorphism in, as indicator of effectiveness of antiobesity agents; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dopamine-transporting, DAT1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Obesity
(genotyping in selection of treatment for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Antiobesity agents
(genotyping in selection of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Monoamines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors of reuptake of, polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Body weight
(loss, therapeutic induction of in treatment of obesity; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(norepinephrine transporter, NET1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Heart rate
(polymorphisms affecting response to antiobesity drugs of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Alleles
Genetic polymorphism
Genotyping (method)
Human
(polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serotonin transporter, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Genetic polymorphism
(single nucleotide; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 9001-66-5
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 50-67-9, Serotonin, biological studies 51-41-2, Norepinephrine 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of reuptake of, polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 135306-42-2 **192374-14-4**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 152316-08-0, GenBank Z29071 154899-20-4, GenBank X76753 165758-41-8, GenBank Z32772 165758-43-0, GenBank Z32774 391536-08-6, GenBank M95167 391548-92-8, GenBank X76758 391548-96-2, GenBank X76762 391772-54-6, GenBank X91127 391854-90-3, GenBank U79746 392067-92-4, GenBank AF050737 398113-85-4, GenBank X91119 398113-92-3, GenBank X91126
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(polymorphisms in genes assocd. with norepinephrine function and their use in the design and selection of therapie)

IT 500753-96-8, 1: PN: WO03018843 SEQID: 1 unclaimed DNA 500753-97-9, 2: PN: WO03018843 SEQID: 2 unclaimed DNA 500753-98-0, 3: PN: WO03018843 SEQID: 3 unclaimed DNA 500753-99-1, 4: PN: WO03018843 SEQID: 4 unclaimed DNA 500754-00-7, 5: PN: WO03018843 SEQID: 5 unclaimed DNA 500754-01-8,

6: PN: WO03018843 SEQID: 6 unclaimed DNA 500754-02-9, 7: PN: WO03018843 SEQID: 7 unclaimed DNA 500754-03-0, 8: PN: WO03018843 SEQID: 8 unclaimed DNA 500754-04-1, 9: PN: WO03018843 SEQID: 9 unclaimed DNA 500754-05-2 500754-06-3 500754-07-4 500754-08-5 500754-09-6 500754-10-9 500754-11-0 500754-12-1 500754-13-2 500754-14-3 500754-15-4 500754-16-5 500754-17-6 500754-18-7 500754-19-8 500754-20-1 500754-21-2 500754-22-3 500754-23-4 500754-24-5 500754-25-6 500754-26-7 500754-27-8 500754-28-9 500754-29-0 500754-30-3 500754-31-4 500754-32-5 500754-33-6 500754-34-7
RL: PRP (Properties)
(unclaimed nucleotide sequence; polymorphisms in genes assocd. with norepinephrine function and their use in the design and selection of therapies)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

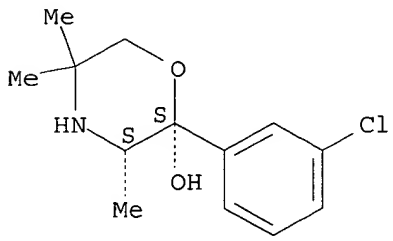
RE

(1) Bertrand; J AM ACAD CHILD ADOLESC PSYCHIATRY 1999, V38(12), P1474
(2) Eriksson; Alcohol 2001, V24(1), P15 CAPLUS
(3) Ho; Annals of Neurology 1995, V37(3), P403 CAPLUS
(4) Mundo; American Journal of Medical Genetics (Neuropsychiatric Genetics) 2000, V96, P379 MEDLINE
(5) Okabe; The Journal of Neuroscience 1999, V19(18), P7781 CAPLUS
(6) Rosmond; Journal of Human Hypertension 2001, V15, P553 CAPLUS
(7) Serritti; Psychiatry Research 2001, V104, P195
(8) Stober; American Journal of Medical Genetics (Neuropsychiatric Genetics) 1996, V67, P523 MEDLINE

IT **192374-14-4**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L25 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:118594 CAPLUS
DN 138:147756
TI Pharmaceutically active morpholinol
IN Ascher, John A.; Johnston, Joseph Andrew; Learned-Coughlin, Susan Marie; Bye, Alan
PA USA
SO U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 886,391.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-537
NCL 514238500
CC 1-11 (Pharmacology)
Section cross-reference(s): 28

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003032643	A1	20030213	US 2002-150341	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		

AB Disclosed is the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and processes for their prepn.; also disclosed is a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, addiction to cocaine or tobacco products, seasonal affective disorder, chronic fatigue, narcolepsy or cognitive impairment using such compd., salts, solvates or compns.

ST morpholinol deriv prepn antidepressant chronic fatigue treatment; seasonal affective disorder treatment morpholinol deriv

IT Mental disorder
(affective, seasonal; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Resolution (separation)
(chromatog.; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Fatigue, biological
(chronic fatigue syndrome; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Mental disorder
(cognitive; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Mental disorder
(depression; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Cognition
(disorder; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Sleep
(narcolepsy; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT Absolute configuration
Antidepressants
Brain
Cognition enhancers
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT **192374-14-4P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT **106083-71-0P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT **192374-15-5P**, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol **233600-52-7P 233600-53-8P**
233600-54-9P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

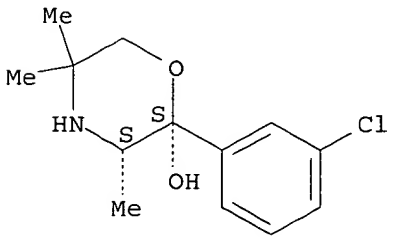
IT 124-68-5, 2-Amino-2-methyl-1-propanol 34841-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT **192374-14-4P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



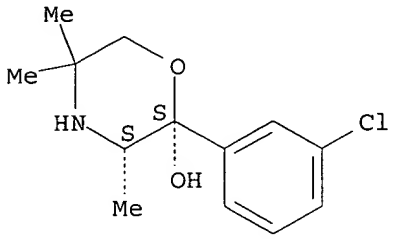
IT **106083-71-0P**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of

action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



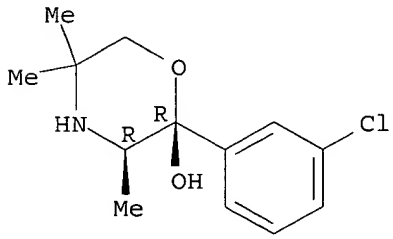
● HCl

IT **192374-15-5P**, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol **233600-52-7P 233600-53-8P 233600-54-9P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

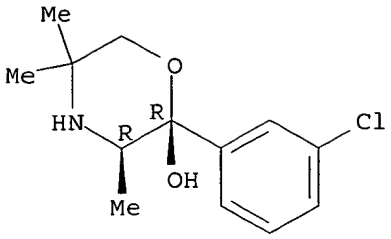
Absolute stereochemistry. Rotation (-).



RN 233600-52-7 CAPLUS

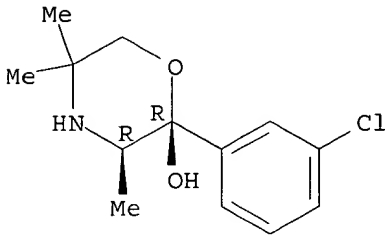
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 233600-53-8 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)-rel- (9CI) (CA INDEX NAME)

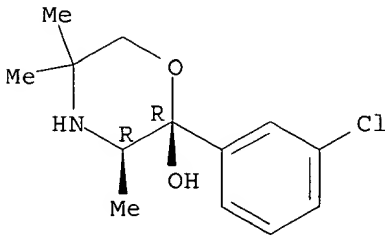
Relative stereochemistry.



● HCl

RN 233600-54-9 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L25 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:23847 CAPLUS
DN 136:79797
TI Bupropion metabolites, and preparation thereof, for treatment of sexual dysfunction
IN Fang, Qun Kevin; Senanayake, Chrisantha Hugh; Grover, Paul
PA Sepracor, Inc., USA
SO U.S., 26 pp., Cont.-in-part of U.S. 510,241.
CODEN: USXXAM
DT Patent

LA English
IC ICM A61K031-535
ICS A61K031-135
NCL 514231200
CC 1-12 (Pharmacology)
Section cross-reference(s): 25, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6337328	B1	20020108	US 2000-640725	20000818
	US 6342496	B1	20020129	US 2000-510241	20000222
	WO 2001062257	A2	20010830	WO 2000-US23080	20000823
	WO 2001062257	A3	20020704		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1259243	A2	20021127	EP 2000-957684	20000823
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	US 2002052340	A1	20020502	US 2001-987930	20011116
	US 2002052341	A1	20020502	US 2001-987931	20011116
PRAI	US 1999-122277P	P	19990301		
	US 1999-148324P	P	19990811		
	US 2000-510241	A2	20000222		
	US 2000-640725	A	20000818		
	WO 2000-US23080	W	20000823		

AB Methods are disclosed which use metabolites of bupropion (prepn. described) for treating sexual dysfunction. Tablet formulations are included.

ST bupropion metabolite prepn sexual dysfunction treatment; tablet pharmaceutical bupropion metabolite sexual dysfunction

IT 5-HT antagonists
(5-HT3; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Antiemetics
Resolution (separation)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Sexual behavior
(disorder; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Sexual behavior
(impotence; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Drug delivery systems
(mucosal; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Drug delivery systems
(oral; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Sexual behavior
(premature ejaculation; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Drug delivery systems
(tablets; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Drug delivery systems
(transdermal; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT Vagina

(vaginal dryness and vaginismus; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 50-67-9, Serotonin, biological studies 51-41-2, Norepinephrine 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 102141-11-7P 102141-12-8P 153365-82-3P 292055-72-2P **357399-43-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT **192374-14-4P 192374-15-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 364-62-5, Metoclopramide 364-62-5D, Metoclopramide, stereoisomers and metabolites 34911-55-2D, Bupropion, metabolites 82801-49-8 83863-69-8, Norcisapride 83863-69-8D, Norcisapride, stereoisomers and metabolites 89565-68-4, Tropisetron 89565-68-4D, Tropisetron, stereoisomers and metabolites 90182-92-6, Zacopride 90182-92-6D, Zacopride, stereoisomers and metabolites 92264-81-8 99614-02-5, Ondansetron 99614-02-5D, Ondansetron, stereoisomers and metabolites 109889-09-0, Granisetron 109889-09-0D, Granisetron, stereoisomers and metabolites 112727-80-7, Renzapride 112727-80-7D, Renzapride, stereoisomers and metabolites 357628-59-2 357628-60-5 386210-40-8 386210-41-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 80478-42-8P 80478-43-9P **106083-71-0P** 292055-71-1P 357628-62-7P 357637-16-2P 357637-18-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 34911-51-8P 92264-82-9P 99102-04-2P 291275-45-1P 291275-46-2P **357399-44-1P** 357628-63-8P 357628-64-9P 386210-39-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 87-69-4, L-Tartaric acid, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 18162-48-6 31677-93-7, Bupropion hydrochloride 32634-66-5, Di-p-toluoyl-L-tartaric acid 34841-35-5 34911-55-2, Bupropion 287477-53-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; bupropion metabolite prepn. for treatment of sexual dysfunction)

RE.CNT 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; CA 977777 1975 CAPLUS
(2) Anon; CA 977778 1975 CAPLUS
(3) Anon; EP 0118036 1984 CAPLUS
(4) Anon; EP 0171227 1986 CAPLUS
(5) Anon; JP 6391352 1988
(6) Anon; WO 9111184 1991 CAPLUS
(7) Anon; EP 0467488 1992 CAPLUS
(8) Anon; WO 9219226 1992 CAPLUS
(9) Anon; WO 9321917 1993 CAPLUS
(10) Anon; WO 9404138 1994 CAPLUS
(11) Anon; WO 9420100 1994 CAPLUS
(12) Anon; WO 9503791 1995 CAPLUS
(13) Anon; WO 9522324 1995 CAPLUS
(14) Anon; WO 9639133 1996 CAPLUS

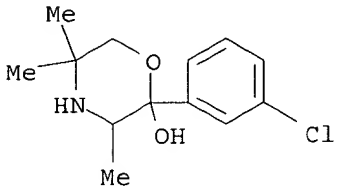
(15) Anon; WO 9729735 1997 CAPLUS
(16) Anon; WO 9850044 1998 CAPLUS
(17) Anon; WO 9937305 1999 CAPLUS
(18) Anon; Neurology, Official Journal of American Academy of Neurology 1984, V34(8)
(19) Anon; Physician's Desk Reference 1998, P1120
(20) Anon; Scrip Bupropion Sustained Release (SR) for Smoking Cessation 1996
(21) Anon; Scrip Itraconazole for pulse dosing of onychomycosis 1996
(22) Anon; Scrip's New Product Review 1990, 50
(23) Applezweig; US 3536809 A 1970 CAPLUS
(24) Ascher, J; J Clin Psych 1995, V56, P395 MEDLINE
(25) Baker; US 4687660 A 1987 CAPLUS
(26) Baker; US 4769027 A 1988
(27) Baker; US RE33994 E 1992
(28) Bannon; Science 1998, V279, P77 CAPLUS
(29) Berger; US 5217987 A 1993 CAPLUS
(30) Bischoff; Eur J Pharmaco 1984, V104, P173 CAPLUS
(31) Blondel-Hill; Drugs 1993, V46(4), P639 MEDLINE
(32) Borowski, T; Brain Res Bull 1993, V30, P607 CAPLUS
(33) Brown; US 4868344 A 1989 CAPLUS
(34) Calabrese, J; Primary Care 1991, V18(2), P421 MEDLINE
(35) Castaldi, G; J Org Chem 1987, V52, P3018 CAPLUS
(36) Castello, R; J Pharm Sci 1962, V51(2), P106
(37) Charney, D; Psychopharmacol Bull 1983, V19(3), P490
(38) Clay; Psychopharma Bull 1988, V24(1), P143 MEDLINE
(39) Coffman; US 4656026 A 1987 CAPLUS
(40) Conners, K; J Am Acad Child Adolesc Psychiatr 1996, V34(10), P1314
(41) Cook, C; J Pharmacy Practice 1997, V10(5), P329
(42) Cooper, B; Neuropsychopharmacology 1994, V11(2), P133 CAPLUS
(43) Cooper, T; Analytical psychopharmacology 1988, P1
(44) Coutts, R; Chirality 1989, V1, P99 CAPLUS
(45) Crenshaw; J Sex Marital Ther 1987, V13(4), P239 MEDLINE
(46) Cusack, B; Psychopharmacol 1994, V114, P559 CAPLUS
(47) Dackis; US 4935429 A 1990 CAPLUS
(48) Dante; US 5512593 A 1996 CAPLUS
(49) Davidson; J Clin Psychiatry 1994, V55(8), P362 MEDLINE
(50) Dilsaver, S; J Clin Psychiatry 1992, V53(7), P252 MEDLINE
(51) Eliel, E; Stereochemistry of Carbon Compounds 1962
(52) Ferris, R; J Clin Psychiatry 1983, V44(5), P74 CAPLUS
(53) Ferris & Beaman; Neuropharmacol 1983, V22(1), P1257
(54) Ferry, L; Circulation 1992, V86, P671
(55) Ferry, L; J Addict, Dis 1994, V13, PA9
(56) Findlay; US 4347178 A 1982 CAPLUS
(57) Findlay; US 4355179 A 1982 CAPLUS
(58) Findlay; US 4356165 A 1982 CAPLUS
(59) Fisher, R; Brain Res Reviews 1989, V14, P245 CAPLUS
(60) Foote; Proconvulsant effect of morphine on seizures induced by pentylenetetrazol in the rat 1984, V105, P179 CAPLUS
(61) Garland; J Psychopharmacology 1998, V12(4), P385 CAPLUS
(62) Gennaro; Remingtons:The Practice of the Science and Pharmacy, 19th ed 1995, P1625
(63) Goetz; Bupropion in Parkinson's Disease, 1984, V34, P1092 MEDLINE
(64) Goodnick, P; Clin Pharmacokinet 1994, V27(4), P307 CAPLUS
(65) Goodnick, P; J Clin Psych 1993, V54(1), P13 MEDLINE
(66) Green, A; J Pharm Pharmacol 1989, V41, P879 CAPLUS
(67) Grimes; Soc Biol Psych 1996, V40, P1184 MEDLINE
(68) Higuchi; US 3630200 A 1971
(69) Hsyu, P; 1997 CAPLUS
(70) Hsyu, P; J Clin Pharmacol 1997, V37(8), P737 CAPLUS
(71) Janowsky, A; J Neurochem 1986, V46, P1272 CAPLUS
(72) Kashman; US 4935439 A 1990 CAPLUS
(73) Kelley, J; J Med Chem 1996, V39, P347 CAPLUS
(74) Ketter, T; J Clin Psychopharmacol 1995, V15(5), P327 MEDLINE
(75) Koppe; US 3622675 A 1971

(76) Laizure, S; Clin Pharmacol Ther 1985, V38, P586 CAPLUS
(77) Lief, H; Am J Psychiatry 1996, V153(3), P442 MEDLINE
(78) Little, K; J Neurochem 1993, V61, P1996 CAPLUS
(79) Ludwig; US 5427798 A 1995 CAPLUS
(80) Martin, P; Pharmacopsychiatry 1990, V23, P187 MEDLINE
(81) McNamee; J Pharm Pharmacol 1986, V37, P147
(82) Mehta; US 3819706 A 1974 CAPLUS
(83) Mehta; US 3885046 A 1975 CAPLUS
(84) Mehta; US 4347176 A 1982 CAPLUS
(85) Merskey, H; J Psychosom Res 1965, V8, P405
(86) Metcalf; US 3960927 A 1976 CAPLUS
(87) Michell, G; Am J Psychiatry 1989, V146(8), P1089
(88) Michell, G; Am J Psychiatry 1989, V146(1), P119 MEDLINE
(89) Moisset, B; Brain Res 1975, V92, P157 CAPLUS
(90) Moret, C; Sensitizing of the response of 5-HT autoreceptors to drugs modifying synaptic availability of 5-HT 1988, V27(1), P43 CAPLUS
(91) Musso; Bioorganic & Medical Chemistry Letters 1997, V7(1), P1 CAPLUS
(92) Musso; Chirality 1993, V5, P495 CAPLUS
(93) Nomikos; Neuropsychopharmacology 1992, V7(1), P7 CAPLUS
(94) Nutt, D; Eur J Pharmacol 1981, V71, P287 CAPLUS
(95) Nutt, D; Neuropharmacology 1980, V19, P1017 CAPLUS
(96) Olsen; PNAS USA 1985; V82, P6701 CAPLUS
(97) Pearlstein; J Clin Psychopharmacol 1997, V17(4), P261 CAPLUS
(98) Peck; US 4393078 A 1983 CAPLUS
(99) Peck; US 4571395 A 1986 CAPLUS
(100) Peck; US 4798826 A 1989 CAPLUS
(101) Phillips; US 4347177 A 1982 CAPLUS
(102) Pinsker; US 5753712 A 1998 CAPLUS
(103) Popli, A; Annals of Clin Psychiatr 1995, V7(2), P99 MEDLINE
(104) Popli, A; J Clin Psych 1994, V55(6), P267 MEDLINE
(105) Posner, J; Eur J Clin Pharmacol 1985, V29, P97 CAPLUS
(106) Potter, W; Clin Neuropharmacol 1990, V13(1), PS45
(107) Roberts; US 4835147 A 1989 CAPLUS
(108) Rose, J; Annu Rev Med 1996, V47, P493 CAPLUS
(109) Rosenstein, D; J Clin Psychiatry 1993, V54(8), P289 MEDLINE
(110) Rudorfer, M; Drug Safety 1994, V10(1), P18 MEDLINE
(111) Ruff; US 5358970 A 1994 CAPLUS
(112) Ruff; US 5541231 A 1996 CAPLUS
(113) Ruff; US 5731000 A 1998 CAPLUS
(114) Ruff; US 5763493 A 1998 CAPLUS
(115) Scharver; US 4347382 A 1982 CAPLUS
(116) Schroeder, D; J Clin Psychiatr 1983, V44(5), P79 CAPLUS
(117) Schroedger, D; The Pharmacologist 1979, V21(3), P191
(118) Seed; US 4895845 A 1990 CAPLUS
(119) Seibyl; US 5447948 A 1995 CAPLUS
(120) Stathis, M; Psychopharmacol 1995, V119, P376 CAPLUS
(121) Stern; US 4347257 A 1982 CAPLUS
(122) Stern; US 4425363 A 1984 CAPLUS
(123) Stern; US 4435449 A 1984 CAPLUS
(124) Stern; US 4438138 A 1984 CAPLUS
(125) Stern; US 4507323 A 1985 CAPLUS
(126) Storrow, A; Am J Emerg Med 1994, V12, P183 MEDLINE
(127) Suckow, R; Drug Metab Disposit 1986, V14(6), P692 CAPLUS
(128) Suckrow, R; Biomedical Chromatog 1997, V11, P174
(129) Sulser, F; Psychopharmacol Bull 1983, V19(3), P300 MEDLINE
(130) Sweet, R; J Clin Pharmacol 1995, V35, P876 CAPLUS
(131) Testa, B; Chirality 1990, V2, P129 CAPLUS
(132) Theeuwes; US 3845770 A 1974 CAPLUS
(133) Theeuwes; US 3916899 A 1975 CAPLUS
(134) Theeuwes; US 4008719 A 1977
(135) Vassout, A; J Receptor Res 1993, V13(1-4), P341 CAPLUS
(136) Wade; Handbook of Pharmaceutical Excipients, 2nd ed 1994, P257
(137) Ward, N; The Management of Pain, Second Edition, Chapter 18 1990, V1, P310

(138) Ward, R; Brain Res 1971, V31, P207 MEDLINE
(139) Welch, R; Nenobiotica 1987, V17(3), P287 CAPLUS
(140) Wilen, S; Tables of Resolving Agents and Optical Resolutions 1972
(141) Wright; J Clin Psych 1985, V46(1), P22 MEDLINE
(142) Zaffaroni; US 3598123 A 1971 CAPLUS
(143) Zarrindast; Gen Pharmacology 1988, V19(2), P201 CAPLUS

IT **357399-43-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

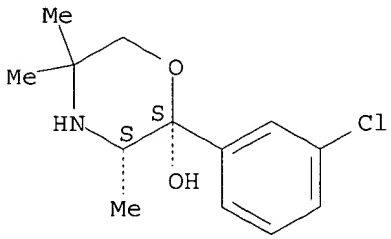
RN 357399-43-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)



IT **192374-14-4P 192374-15-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

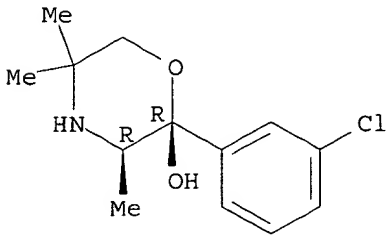
RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



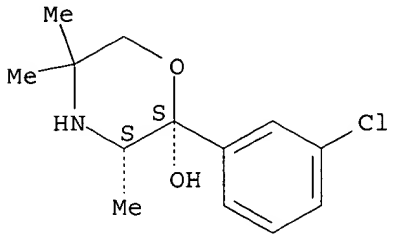
IT **106083-71-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolite prepn. for treatment of sexual dysfunction)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

IT **357399-44-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; bupropion metabolite prepn. for treatment of sexual dysfunction)

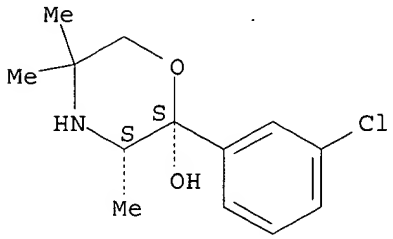
RN 357399-44-1 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 192374-14-4
CMF C13 H18 Cl N O2

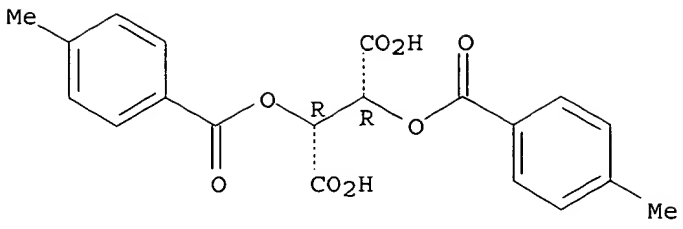
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

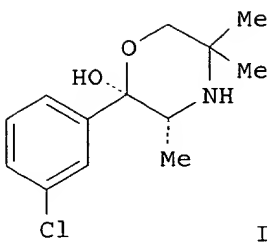
Absolute stereochemistry.



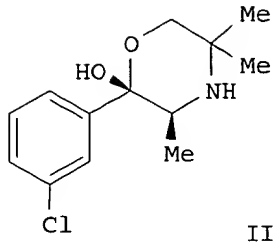
L25 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:635898 CAPLUS
DN 135:211043
TI Synthesis of bupropion metabolites and their use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake
IN Fang, Qun K.; Senanayake, Chrisantha H.; Grover, Paul
PA Sepracor Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-5375
ICS A61K031-137; A61P025-24; A61P025-34; A61P025-20
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001062257	A2	20010830	WO 2000-US23080	20000823
	WO 2001062257	A3	20020704		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6342496	B1	20020129	US 2000-510241	20000222
	US 6337328	B1	20020108	US 2000-640725	20000818
	EP 1259243	A2	20021127	EP 2000-957684	20000823
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI	US 2000-510241	A	20000222		
	US 2000-640725	A	20000818		
	US 1999-122277P	P	19990301		
	US 1999-148324P	P	19990811		
	WO 2000-US23080	W	20000823		

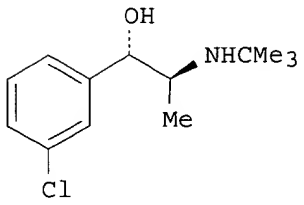
GI



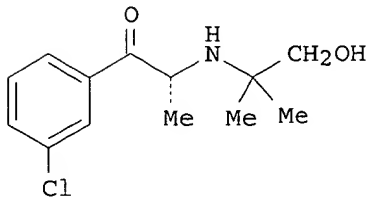
I



II



III



IV

AB Methods and compns. are disclosed which utilize metabolites of bupropion, including optically pure metabolites, e.g. I, II, III and IV, for treating disorders ameliorated by inhibition of neuronal monoamine reuptake, such as, sexual dysfunction, affective disorders, cerebral function disorders, cigarette smoking, and urinary incontinence. Thus, III was prepd. from racemic bupropion hydrochloride via borane redn.; resoln. of the racemic threo deriv. with L-tartaric acid to isolate the (R,R)-stereoisomer as the L-tartrate salt; treatment of supernatant with D-tartaric acid to give the (S,S)-stereoisomer as the D-tartrate salt; and hydrolysis of the latter to give III. III was tested for inhibition of inhibition of 5-HT reuptake [insignificant results, IC50 = 229 nM (nH = 0.8)].

ST bupropion metabolite prepn neuronal monoamine reuptake inhibitor; sexual dysfunction treatment bupropion metabolite; cerebral function disorder treatment bupropion metabolite; cigarette smoking disorder treatment bupropion metabolite; incontinence treatment bupropion metabolite

IT 5-HT antagonists
(5-HT3, adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Muscarinic receptors
Nicotinic receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonists, adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Brain
(cerebral dysfunction, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Tobacco products
(cigarettes, nicotine addiction, medicaments; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Mental disorder
(depression, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Sexual behavior
(disorder, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine

reuptake)

IT Sexual behavior
(impotence, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Bladder
(incontinence, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Alzheimer's disease
Epilepsy
Parkinson's disease
(medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Sleep
(narcolepsy, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Monoamines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neuronal, reuptake inhibitor; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 5-HT antagonists
(serotonin reuptake inhibitor adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Analgesics
Anti-inflammatory agents
Anticonvulsants
Antidepressants
Drug delivery systems
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 54-11-5, Nicotine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT **357399-44-1P** 357628-61-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 80478-42-8P 80478-43-9P 92264-82-9P 99102-04-2P 102141-11-7P 102141-12-8P 153365-82-3P **192374-14-4P** 292055-72-2P 357628-62-7P 357628-64-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 31677-93-7 34911-55-2, (.+-.)-Bupropion
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 34911-55-2DP, Bupropion, metabolites and derivs. **106083-71-0P**
192374-15-5P 233600-54-9P 292055-71-1P 357399-46-3P
357399-47-4P 357628-59-2P 357628-60-5P 357628-63-8P 357637-16-2P
357637-18-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 75-64-9, tert-Butylamine, reactions 87-69-4, L-Tartaric acid, reactions
124-68-5, 2-Amino-2-methyl-1-propanol 147-71-7, D-Tartaric acid
32634-66-5 32634-68-7 34841-35-5, 1-(3-Chlorophenyl)-1-propanone
287477-53-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone 291275-45-1P 291275-46-2P
357399-43-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT **357399-44-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

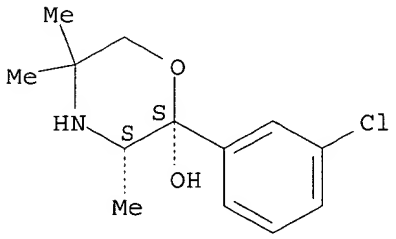
RN 357399-44-1 CAPLUS

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 192374-14-4
CMF C13 H18 Cl N O2

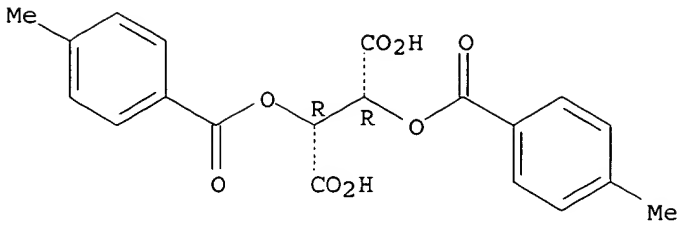
Absolute stereochemistry. Rotation (+).



CM 2

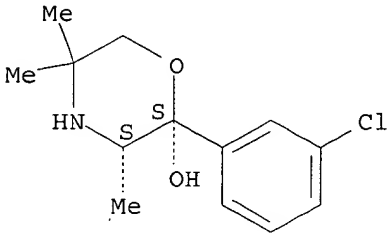
CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry.



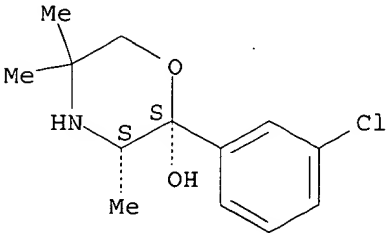
IT **192374-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **106083-71-0P 192374-15-5P 233600-54-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
RN 106083-71-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

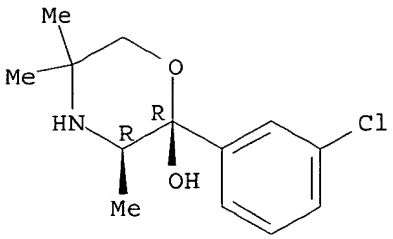
Absolute stereochemistry. Rotation (+).



● HCl

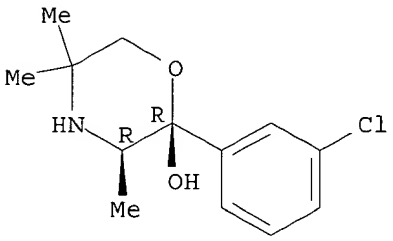
RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



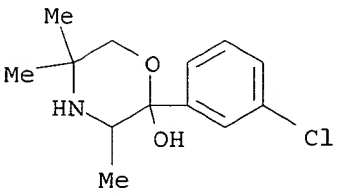
RN 233600-54-9 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

IT **357399-43-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
RN 357399-43-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)



L25 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:836391 CAPLUS
DN 134:147365
TI Rapid access to enantiopure bupropion and its major metabolite by stereospecific nucleophilic substitution on an .alpha.-keto triflate
AU Fang, Q. K.; Han, Z.; Grover, P.; Kessler, D.; Senanayake, C. H.; Wald, S. A.
CS Chemical Process Research and Development, Sepracor Inc., Marlborough, MA, 01752, USA
SO Tetrahedron: Asymmetry (2000), 11(18), 3659-3663

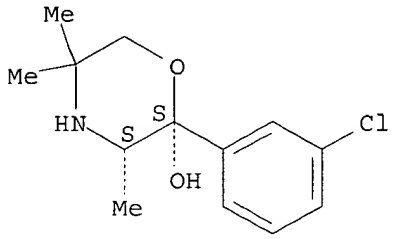
CODEN: TASYE3; ISSN: 0957-4166
PB Elsevier Science Ltd.
DT Journal
LA English
CC 25-16 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 63
OS CASREACT 134:147365
AB A stereospecific method for the synthesis of enantiopure .alpha.-amino ketone from its corresponding .alpha.-hydroxy ketone via a triflate intermediate is discussed. This strategy provides a rapid and efficient route for the prepn. of either enantiomer of bupropion and its biol. active hydroxylated metabolite. To a soln. of (2R)-1-(3-chlorophenyl)-2-hydroxy-1-propanone (0.30 g) in dichloromethane (6 mL) was added trifluoromethanesulfonic acid anhydride (0.50 g) at -78.degree.; then, lutidine (0.26 g) was added. The intermediate trifluoromethanesulfonic acid (1R)-2-(3-chlorophenyl)-1-methyl-2-oxoethyl ester (.alpha.-keto triflate) was not isolated. The reaction mixt. was allowed to warm to -40.degree. and stirred at that temp. for 40 min before 2-amino-2-methyl-1-propanol (0.40 g) was added. This mixt. was stirred at -40.degree. for 2 h, warmed to 0.degree. and stirred overnight. After work-up, the product, (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol, was obtained in 65% yield and 98% enantiomeric excess.
ST stereoselective nucleophilic substitution keto triflate; trifluoromethanesulfonate chlorophenyloxoethyl prepn nucleophilic substitution; propanone trifluoromethylsulfonyloxy stereochem nucleophilic substitution aminopropanol; chlorophenyl morpholinol bupropion metabolite prepn; bupropion Wellbutrin prepn
IT Stereochemistry
(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)
IT Substitution reaction, nucleophilic
(stereoselective; prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)
IT 75-64-9, tert-Butylamine, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 358-23-6, Trifluoromethanesulfonic acid anhydride 287477-53-6 291275-46-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)
IT **192374-14-4P**, (+)-(2S,3S)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol **192374-15-5P**, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 324548-43-8P, (S)-Bupropion 324548-45-0P, (S)-Bupropion hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adam, W; J Am Chem Soc 1998, V120, P708 CAPLUS
(2) Boswell, G; J Heterocycl Chem 1997, V34, P1813 CAPLUS
(3) Bradshaw, C; J Org Chem 1992, V57, P1526 CAPLUS
(4) Coppola, G; .alpha.-Hydroxy Acids in Enantioselective Synthesis 1997
(5) Creary, X; J Am Chem Soc 1984, V106, P5568 CAPLUS
(6) Davis, F; Chem Rev 1992, V92, P919 CAPLUS
(7) Davis, F; J Am Chem Soc 1990, P6679 CAPLUS
(8) Duh, T; Tetrahedron: Asymmetry 1993, V4, P1793 CAPLUS
(9) Effenberger, F; Liebigs Ann Chem 1986, P334 CAPLUS
(10) Giordani, A; Tetrahedron: Asymmetry 1997, V8, P253 CAPLUS
(11) Hashiyama, T; J Org Chem 1992, V57, P5067 CAPLUS
(12) Hashiyama, T; J Org Chem 1992, V57, P5067 CAPLUS

(13) Kelley, J; J Med Chem 1996, V39, P347 CAPLUS
(14) Kunz, H; Angew Chem 1984, V84, P798
(15) Liu, A; J Med Chem 1992, V35, P2113 CAPLUS
(16) Mey, B; Chirality 1998, P307 CAPLUS
(17) Musso, D; Bioorg Med Chem Lett 1997, P1 CAPLUS
(18) Musso, D; Chirality 1993, V5, P495 CAPLUS
(19) Suckow, R; Biomed Chromatogr 1997, V11, P174 CAPLUS
(20) Welch, R; Xenobiotica 1987, V17, P287 CAPLUS
(21) Zhu, Y; J Am Chem Soc 1999, V121, P4080 CAPLUS
(22) Zhu, Y; Tetrahedron Lett 1998, V39, P7819 CAPLUS

IT **192374-14-4P**, (+)-(2S,3S)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol **192374-15-5P**, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)

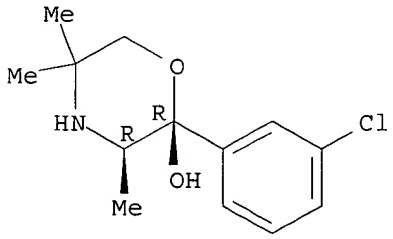
RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:627938 CAPLUS
DN 133:227784
TI Bupropion metabolites and methods of their synthesis and therapeutic uses and compositions
IN Jerussi, Thomas P.; McCullough, John R.; Senanayake, Chrisantha H.; Fang, Qun K.
PA Sepracor Inc., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English

ICI A61
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 25
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000051546	A2	20000908	WO 2000-US5109	20000229
	WO 2000051546	A3	20010111		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2000035055	A5	20000921	AU 2000-35055	20000229
PRAI	US 1999-122777P	P	19990301		
	US 1999-148324P	P	19990811		
	WO 2000-US5109	W	20000229		

OS MARPAT 133:227784

AB Methods and compns. are disclosed which utilize metabolites of bupropion for treating disorders ameliorated by inhibition of neuronal monoamine reuptake. Such disorders include, but are not limited to, erectile dysfunction, affective disorders, cerebral function disorders, cigarette smoking, and incontinence. The invention further discloses methods of making optically pure bupropion metabolites.

ST bupropion metabolite synthesis treatment monoamine reuptake disorder; erectile dysfunction treatment bupropion metabolite; affective disorder treatment bupropion metabolite; cigarette smoking treatment bupropion metabolite; incontinence treatment bupropion metabolite; optically pure bupropion metabolite

IT 5-HT antagonists
(5-HT3, adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Antiemetics
(adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Mental disorder
(affective, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Anticonvulsants
Antidepressants
Antiparkinsonian agents
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(capsules; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Brain, disease
(cerebrum, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Mental disorder
(depression, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Sexual behavior
(impotence, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Bladder
(incontinence, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(mucosal; bupropion metabolites and methods of synthesis and

therapeutic uses and compns.)

IT Sleep
(narcolepsy, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(oral; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Behavior
(smoking, cessation of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(solids; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(solns.; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(tablets; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(transdermal patches; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems
(transdermal; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Nerve
(treating disorder ameliorated by inhibition of monoamine reuptake in; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Monoamines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(treating disorder ameliorated by inhibition of neuronal reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Epilepsy
Parkinson's disease
(treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Biological transport
(uptake, treating disorder ameliorated by inhibition of neuronal monoamine reuptake; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 364-62-5, Metoclopramide 89565-68-4, Tropisetron 90182-92-6, Zacopride 99614-02-5, Ondansetron 109889-09-0, Granisetron 112727-80-7, Renzapride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 34911-55-2, Bupropion 119802-68-5 292055-72-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 153365-82-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 102141-12-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 358-23-6, Trifluoromethane sulfonic anhydride
RL: NUU (Other use, unclassified); USES (Uses)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 34841-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 291275-45-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 287477-53-6P 291275-46-2P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT **192374-15-5P** 292055-71-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 34911-55-2DP, Bupropion, metabolites
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 291275-47-3 291275-48-4 291275-49-5 291275-50-8 291275-51-9 291275-52-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 51-41-2, Norepinephrine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 50-67-9, Serotonin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(second pharmacol. active compds. of inhibitors of reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

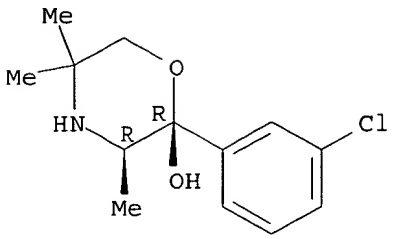
IT 51-61-6, Dopamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(treating disorder ameliorated by inhibition of neuronal reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 54-11-5, Nicotine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of addiction to; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT **192374-15-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:487216 CAPLUS
DN 131:111445
TI Pharmaceutically active morpholinol
IN Morgan, Phillip Frederick; Musso, David Lee; Partridge, John Joseph
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-535
CC 1-11 (Pharmacology)
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9937305	A1	19990729	WO 1999-US1134	19990120
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2318268	AA	19990729	CA 1999-2318268	19990120
	AU 9923280	A1	19990809	AU 1999-23280	19990120
	AU 755536	B2	20021212		
	BR 9907203	A	20001017	BR 1999-7203	19990120
	EP 1047428	A1	20001102	EP 1999-903200	19990120
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 200000438	A	20011217	EE 2000-438	19990120
	JP 2002501025	T2	20020115	JP 2000-528287	19990120
	NZ 505809	A	20020927	NZ 1999-505809	19990120
	NO 2000003721	A	20000919	NO 2000-3721	20000720
	HR 2000000494	A1	20001231	HR 2000-494	20000721
PRAI	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		
	WO 1999-US1134	W	19990120		

AB Disclosed are the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, or addiction to cocaine or nicotine-contg. (esp. tobacco) products using such compd., salts, solvates or compns.

ST bupropion metabolite morpholinol dextro enantiomer antidepressant
IT Mental disorder

(attention deficit hyperactivity disorder; pharmaceutically active morpholinol compd.)

IT Sexual behavior
(disorder; pharmaceutically active morpholinol compd.)

IT Analgesics
Anti-Alzheimer's agents
Antidepressants
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents
Drug dependence
(pharmaceutically active morpholinol compd.)

IT **106083-71-0P 192374-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(pharmaceutically active morpholinol compd.)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol compd.)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone **233600-52-7P** **233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol compd.)

IT **192374-15-5P 233600-54-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pharmaceutically active morpholinol compd.)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

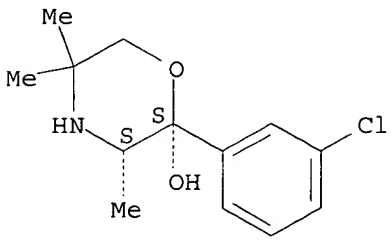
(1) Kelley; J Med Chem 1996, V39(2), P347 CAPLUS
(2) Martin, P; Pharmacopsychiatry 1990, V23(4), P187 MEDLINE

IT **106083-71-0P 192374-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(pharmaceutically active morpholinol compd.)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

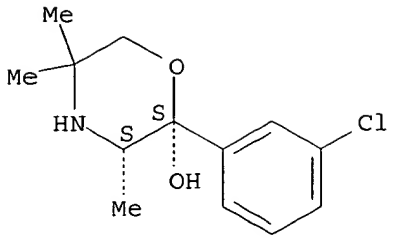


● HCl

RN 192374-14-4 CAPLUS

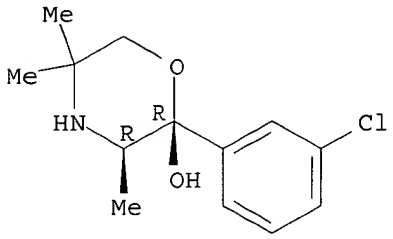
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



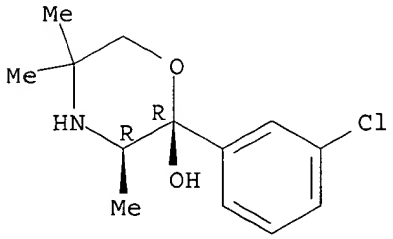
IT **233600-52-7P 233600-53-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pharmaceutically active morpholinol compd.)
RN 233600-52-7 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 233600-53-8 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)-rel- (9CI) (CA INDEX NAME)

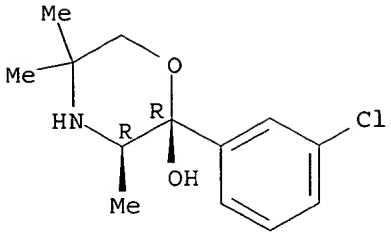
Relative stereochemistry.



● HCl

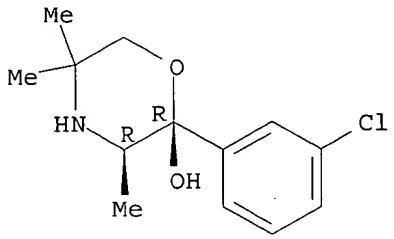
IT **192374-15-5P 233600-54-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pharmaceutically active morpholinol compd.)
RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 233600-54-9 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L25 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:375543 CAPLUS
DN 127:103838
TI Enantiomeric determination of the phenylmorpholinol metabolite of bupropion in human plasma using coupled achiral-chiral liquid chromatography
AU Suckow, Raymond F.; Zhang, Ming F.; Cooper, Thomas B.
CS Analytical Psychopharmacology Division, New York State Psychiatric Institute, New York, NY, 10032, USA
SO Biomedical Chromatography (1997), 11(3), 174-179
CODEN: BICHE2; ISSN: 0269-3879
PB Wiley
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A coupled achiral-chiral stationary phase liq. chromatog. technique was developed to sep. and quantitate the enantiomers of the phenylmorpholinol metabolite (2) of the antidepressant bupropion (1) in human plasma. At the retention time of 2, a switching valve loaded a portion of the eluting compd. onto a protein-bonded chiral stationary phase which resolved 2 into the (+) (-) stereoisomers using an aq. mobile phase of potassium phosphate (pH=6.25) and 5% 2-propanol. All eluting compds. were monitored using UV detection at 214 nm, and no plasma endogenous material or other commonly used psychotropic drugs were found to interfere. Within-day and between-day variations were less than 6% over the expected concn. range, and a limit of quantitation of about 125 ng/mL of 2 was obsd. Steady-state plasma samples from 17 patients receiving 1 were found to contain the (-) enantiomer to the extent of about 96% of total 2. The potential clin. implications of these results are not known since all previous pharmacol. studies were carried out with the racemic 2.
ST bupropion phenylmorpholinol metabolite enantiomer detn plasma; liq

chromatog bupropion metabolite enantiomer detn

IT Blood analysis
Resolution (separation)
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

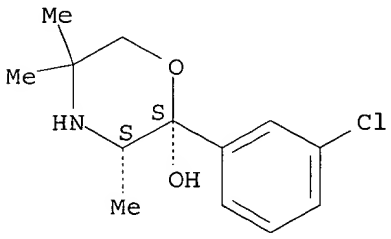
IT **192374-14-4 192374-15-5**
RL: ANT (Analyte); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

IT 31677-93-7, Bupropion hydrochloride
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

IT **192374-14-4 192374-15-5**
RL: ANT (Analyte); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

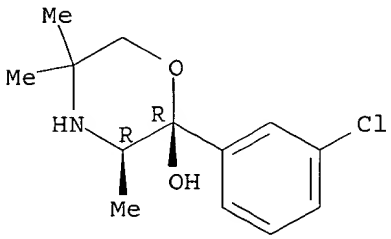
RN 192374-14-4 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

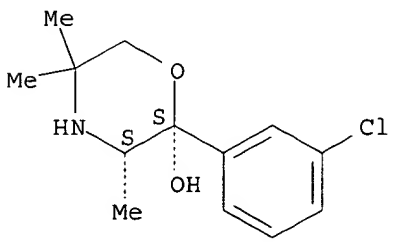
Absolute stereochemistry. Rotation (-).



L25 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:6865 CAPLUS
DN 124:146028
TI (2S,3S,5R)-2-(3,5-Difluorophenyl)-3,5-dimethyl-2-morpholinol: A Novel Antidepressant Agent and Selective Inhibitor of Norepinephrine Uptake
AU Kelley, James L.; Musso, David L.; Boswell, G. Evan; Soroko, Francis E.; Cooper, Barrett R.

CS Division of Organic Chemistry, Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SO Journal of Medicinal Chemistry (1996), 39(2), 347-9
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
AB The title compd. was prepd. in four steps from 3,5-difluorobenzonitrile. The pharmacol. profile of (2S,3S,5R)-2-(3,5-difluorophenyl)-3,5-dimethyl-2-morpholinol suggests that it will display antidepressant activity which involves inhibition of the norepinephrine uptake mechanism without the cholinergic or cardiac depression effects assocd. with tricyclic antidepressants.
ST norepinephrine difluorophenyl dimethyl morpholinol prepn; antidepressant difluorophenyl dimethyl morpholinol prepn
IT Antidepressants
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)
IT **106083-71-0**, BW 306U
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of)
IT 135306-39-7P 135306-42-2P, BW 1555U88 135306-47-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)
IT 64248-63-1, 3,5-Difluorobenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)
IT 135306-45-5P, 1-(3,5-Difluorophenyl)-1-propanone 135306-46-6P, 2-Bromo-1-(3,5-difluorophenyl)-1-propanone 173069-02-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)
IT **106083-71-0**, BW 306U
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of)
RN 106083-71-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

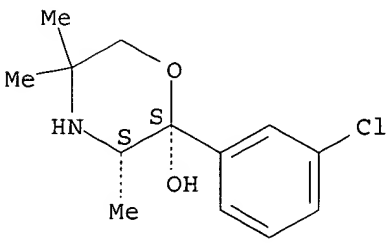
Absolute stereochemistry. Rotation (+).



● HCl

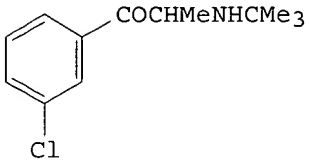
L25 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1987:400205 CAPLUS
DN 107:205
TI Pharmacological significance of the species differences in bupropion metabolism
AU Welch, Richard M.; Lai, Allen A.; Schroeder, David H.
CS Wellcome Res. Lab., Research Triangle Park, NC, 27560, USA
SO Xenobiotica (1987), 17(3), 287-98
CODEN: XENOBH; ISSN: 0049-8254
DT Journal
LA English
CC 1-2 (Pharmacology)
AB Bupropion was previously shown to provide a dose-dependent prevention of tetrabenazine-induced sedation in mice but not rats. Bupropion was extensively metabolized in mice, rats, dogs and man. About 85% of the dose was excreted in the urine of rats and man. The predominant metabolites in rat urine were side chain cleavage products of bupropion [m-chlorobenzoic acid] with a minor fraction consisting of basic side chain hydroxylated metabolites. Mice, dogs and man form a major side chain hydroxylated product BW 306U which appeared in higher concns. than bupropion in plasma of these species but not rats. The relatively high plasma levels of BW 306U in mice but not rats may account for the species difference in pharmacol. response obsd. with bupropion.
ST bupropion metab species; antidepressant action bupropion species
IT Mental disorder
(depression, inhibition of, species difference in bupropion metab. in humans and lab. animals in relation to)
IT 535-80-8, m-Chlorobenzoic acid 34911-55-2D, Bupropion, glucuronide conjugates 57728-59-3 80478-42-8 80478-43-9 **106083-71-0**, B.W. 306U
RL: FORM (Formation, nonpreparative)
(formation of, as bupropion metabolite, in humans and lab. animals, species differences in)
IT 34911-55-2, Bupropion
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of, in humans and lab. animals, species differences in, pharmacol. significance of)
IT **106083-71-0**, B.W. 306U
RL: FORM (Formation, nonpreparative)
(formation of, as bupropion metabolite, in humans and lab. animals, species differences in)
RN 106083-71-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

L25 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1987:43388 CAPLUS
DN 106:43388
TI Pharmacokinetics of bupropion and metabolites in plasma and brain of rats, mice, and guinea pigs
AU Suckow, Raymond F.; Smith, Thomas M.; Perumal, Arthur S.; Cooper, Thomas B.
CS Dep. Anal. Psychopharmacol., New York State Psychiatr. Inst., Orangeburg, NY, 10962, USA
SO Drug Metabolism and Disposition (1986), 14(6), 692-7
CODEN: DMDSAI; ISSN: 0090-9556
DT Journal
LA English
CC 1-2 (Pharmacology)
GI



I

AB Rats, mice, and guinea pigs were used as animal models to evaluate bupropion (I) metab. The pharmacokinetics of bupropion and its major basic metabolites, BW 306U and BW A494U, were detd. by liq chromatog. following i.p. administration of 40 mg/kg bupropion. Further investigation of the reduced bupropion metabolite BW A494U was carried out by the i.p. administration of this metabolite to these animals and assaying the plasma and brain samples 90 min after dosing. Anal. of the pharmacokinetic data revealed that the rat quickly metabolized bupropion, but no basic metabolites accumulated. The mouse metabolized bupropion predominantly to BW 306U, whereas the guinea pig converted bupropion to reduced bupropion (BW A494U) as well as BW 306U. Brain to plasma ratios of bupropion among these animals did not vary significantly. However, both metabolites showed dramatic differences in their brain to plasma ratios among these species. When BW A494U was injected, almost 3% of the plasma concn. of BW A494U was detd. to be bupropion in the rat. Lesser amts. were converted in the mouse and guinea pig than in the rat. Therefore, distinct differences exist in the metab. of bupropion in various species of animals. The guinea pig, when compared to the rat or mouse, appears to constitute a model that most closely resembles that of human bupropion metab.

ST bupropion metabolite pharmacokinetics plasma brain
IT Blood plasma
Brain, metabolism
(bupropion pharmacokinetics in)
IT 80478-42-8 **106083-71-0**
RL: PROC (Process)
(as bupropion metabolite, pharmacokinetics of)
IT 34911-55-2, Bupropion
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of)
IT **106083-71-0**
RL: PROC (Process)
(as bupropion metabolite, pharmacokinetics of)
RN 106083-71-0 CAPLUS
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)